Lioresal

LIORESAL (baclofen) is Ciba-Geigy's antispasticity agent 4-amino-3-(*p*-chlorphenyl) butyric acid. The drug appears to affect reflex pathways in the spinal cord. It is most useful for the symptomatic reduction of clonus, muscle tightness and aching, "jumping of legs" at night, and flexor or extensor spasms (such as during transfers from wheelchair to bed) arising from spinal cord damage due to trauma or multiple sclerosis (MS). It has little efficacy for spasticity of cerebral origin and induces more adverse effects in older patients compared with youths. It is not a curative drug for multiple sclerosis.

Adverse clinical effects are (in order of frequency of occurrence) drowsiness which usually occurs during initiation of therapy, dizziness, increased weakness, nausea, fatigue, headache, insomnia and possibly increased constipation. Since many of these symptoms are also associated with underlying disease process (multiple sclerosis, for example) caution must be exercised in attributing adverse reactions to the drug. Gradual withdrawal and subsequent reinstitution of the drug may be necessary to show cause and effect. Interaction with sedatives and alcohol occurs. The agent is not approved for use in children or pregnant or lactating women. The product insert (prescribing information) suggests starting dosage at 5 mg three times a day for three days, then gradually increasing to 20 mg three times a day. I often start at 5 mg given at bedtime for three to five days and then gradually increase the dosage. Some patients with MS seem exquisitely sensitive to the drug. Also starting with a dose given at bedtime significantly decreases complaints of drowsiness.

Close supervision of the patient is necessary because he may be using his spasticity to hold up his head or to stand during transfers. As the spasticity decreases, weakness may become severe and the patient will choose to stop the medication. Sometimes 10 mg a day is sufficient to give some benefit—one should be aware of individual variation in response and adverse effects. Asymmetry of response is seen sometimes. In general, less severe spasticity responds better than long-standing severe tightness. Occasionally the response is dramatic; at times only slight relief of muscle pain is achieved. When withdrawing the medications, do so slowly because rebound spasticity and hallucinations can occur.

Occasionally improvement in urinary tract function will be seen. A use for baclofen which is not mentioned in the product insert is as a treatment for trigeminal neuralgia. I have used it in patients allergic to dilantin or carbamazepine.

In summary, baclofen is a unique new drug that, if used carefully, offers significant relief of disabling spasticity, particularly in patients with MS.

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Migraine in Children

MIGRAINE IN CHILDREN may appear as the classical syndrome, beginning with painless preheadache phenomena manifested primarily as defects in visual function, followed thereafter by typical hemicranial pounding pain with associated nausea, vomiting and prostration. In addition, some migrainous episodes may occur in childhood in a considerably more recondite manner. Ehyai and Fenichel have described the cases of five patients with acute confusional migraine in which the primary complaint was confused agitation resembling a toxic metabolic psychosis. This syndrome occurred in either sex between the ages of 5 and 16 years. An acute confusional state was the initial manifestation of one of their migrainous patients, and in several children with this syndrome in previous reports. In the absence of a history of migraine there is considerable difficulty in making the diagnosis and therefore a family history of migraine becomes an important clue.

Headache may not be reported as a part of the acute confusional migraine syndrome, but typical migraine headaches always develop eventually. Confusion and disorientation are accompanied by agitation, a mixture of apprehension and combativeness. The duration of an attack is usually several hours but may be as brief as ten minutes or as long as twenty hours. The episode usually terminates in a deep sleep and the children appear to be normal on awakening. Of the five patients in the report by Ehyai and Fenichel, four had recurrent episodes of acute confusional migraine that tended to cluster over a relatively brief period of days or months. The mechanism is believed to be cerebral ischemia of one or both hemispheres.

In general, no specific therapy is required for acute confusional migraine beyond reassurance of the family and patient of the benign nature of the attack and its relationship to the migraine process. Ergot compounds are not necessarily helpful since many of the complaints are thought to be related to intracranial vasoconstriction. Should vascular headache appear subsequent to the development of acute confusional migraine, ergot compounds in standard doses can be employed.

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Epsilon-Aminocaproic Acid for Subarachnoid Hemorrhage

EPSILON-AMINOCAPROIC ACID (EACA, Amicar) has been shown to be effective in reducing the frequency of renewed bleeding in patients with subarachnoid hemorrhage. This drug is an inhibitor of fibrinolysis and probably acts by inhibiting the synthesis of plasmin from plasminogen and also the direct effect of plasmin. It probably acts by competitive inhibition of the activator that converts plasminogen into active plasmin. In a cooperative study, Nibbelink and co-workers documented the effectiveness of EACA in decreasing the frequency of renewed bleeding in patients with subarachnoid hemorrhage. Chowdhary and associates also showed in a controlled clinical trial that EACA was effective in reducing immediate recurrence of spontaneous subarachnoid hemorrhage. There have been some reports indicating that EACA may not be effective, but most of these studies have only included a few patients, and often they did not use controls.

EACA is used during the first two weeks of a subarachnoid hemorrhage while waiting for surgical therapy, if such is considered possible and indicated. It is during the first two weeks that recurrent hemorrhage or renewed bleeding is most likely, probably in part because of increased plasminogen levels in the cerebrospinal fluid at this time. EACA should be used carefully and fibrinolytic assays may possibly be helpful in monitoring the therapy.

EACA is usually given at 1 gram every hour orally or through a nasogastric tube or intravenously by constant infusion. When given intravenously it should be given slowly, otherwise it may induce significant hypotension, arrhythmias or bradycardias. The most common side effects are nausea, diarrhea and vomiting. Less likely to occur are dizziness, nasal stuffiness, headache or rash. There have been some cases of mild to moderate muscle tenderness or necrosis (or both) associated with its use. There have been a number of complications possibly associated with EACA therapy; however, because patients are ill and bedridden it is uncertain if the frequency or the actual cause of the side effects can definitely be attributed to the EACA therapy. Such possible complications may include intracranial vascular thrombosis, arteriolar-capillary fibrin thrombi or extracranial vascular thrombosis such as in the coronary, gastrointestinal or renal vessels. The occurrence of pulmonary emboli originating from deep vein thrombosis has also been considered to be a side effect of the drug. Possible confirmation of these complications has been made in some cases by biopsy or autopsy material.

If EACA is used carefully and appropriately, it will have a significant therapeutic benefit in reducing the initial morbidity and mortality in this life-threatening situation.

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Evoked Cerebral Potentials

EVOKED CEREBRAL POTENTIALS recorded by newer computer techniques have recently become a widely used means of documenting, discovering and further defining lesions in the central nervous system. Tests are now available for examining visual, auditory and somatosensory (posterior column) pathways. Frequently, lesions show up on evoked potential tests but not on any other tests. Indeed, sometimes *silent* lesions are found despite a normal physical examination and history for that pathway.

A major use of evoked potentials is to find demyelinating lesions. These show up as delays in the time between the stimulation and a measured brain electrical response. In cases of suspected multiple sclerosis (MS) about half of the patients with no known brain stem problems nevertheless have abnormal brain stem auditory evoked potentials. Likewise, about half of these patients